

In re application of: Lonnie O. Ingram et al.  
Application No.: 09/885,294  
Group No.: 1651  
Filed: June 19, 2001  
Response to Office Action

## **REMARKS**

Claims 1-55 are pending in the application, with claims 2, 5, 14-17, 34, 35 and 43-55 having been withdrawn from consideration as directed to a non-elected invention. Claims 1, 3, 9, 18, 19, 21-25, 27, 29-31, 33, 38 and 42 have been amended and claims 2, 5, 12-17, 20, 34, 35, 43-55 have been canceled without prejudice or disclaimer. No new matter has been added. Accordingly, claims 1, 3, 4, 6-11, 18, 19, 21-33, and 36-42 will be pending in the application upon entry of this amendment. For the Examiner's convenience, a clean set of the claims that will be pending in the application is attached hereto as Appendix A.

Amendment and cancellation of the claims are not to be construed as an acquiescence to any of the rejections/objections set forth in the instant Office Action, and were done solely to expedite prosecution of the application. Applicants reserve the right to pursue the claims as originally filed, or substantially similar claims, in this or one or more continuation patent applications.

### ***Restriction Requirement***

Page 2 of the Office Action indicates that the restriction requirement has been made final. In view of the finality of the restriction requirement, claims 2, 5, 14-17, 34, 35 and 43-55 have been cancelled as directed to non-elected subject matter. Applicants hereby reserve the right to pursue the subject matter of the cancelled claims in one or more divisional patent applications.

### ***Claims Rejections – 35 U.S.C. §112, First Paragraph***

Claim 9 is rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification, at pages 3 and 14, has been amended to include the ATCC accession numbers for *K. oxytoca* M5A1 and LY01, as well as the dates of deposits for all deposits, the

In re application of: Lonnie O. Ingram et al.  
Application No.: 09/885,294  
Group No.: 1651  
Filed: June 19, 2001  
Response to Office Action

complete taxonomic description for LY01, and the name and address of the depository. Claim 9 has been amended to include the ATCC accession numbers for *K. oxytoca* M5A1 and LY01 as well as the taxonomic description of LY01.

The undersigned hereby avers that the deposits recited in the specification at pages 3 and 14 and in claim 9 have been accepted for deposit under the Budapest Treaty and that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent. In support of this statement, Applicants enclose copies of the ATCC deposit receipts. In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection.

***Claims Rejections – 35 U.S.C. §112, Second Paragraph***

Claims 1, 3-4, 6-13, 18-33, and 36-42 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner alleges that claim 1 is incomplete "in the absence of a recovery step for the product produced." Applicants respectfully disagree and traverse the rejection.

Applicants note that the claimed methods are methods for *increasing* production of alcohol from a saccharide source by an alcohologenic cell, and not producing alcohol. Alcohologenic cells, by definition, produce alcohol. Recovering the ethanol is not a necessary step of the invention. Indeed, the ethanol produced can be further processed/reacted without actual recovery. More importantly, addition to the claims of the recitation of a step of recovering the alcohol would unnecessarily limit the claims. If such a step were added, an infringer could avoid infringing the claim simply by not recovering the alcohol produced, even though the infringer will have carried out all the essential steps of the claim.

In re application of: Lonnie O. Ingram et al.  
Application No.: 09/885,294  
Group No.: 1651  
Filed: June 19, 2001  
Response to Office Action

The claims as written recite all the steps necessary to carry out the invention. As such, the claims adequately set forth the metes and bounds of the invention and give fair notice as to what one must do in order to infringe the claims. The second paragraph of 35 U.S.C. §112 requires nothing more. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claim 1 is also rejected as being vague and indefinite in that the extent of 'increasing' production cannot be readily ascertained. Applicants respectfully disagree and traverse.

Applicants have fully described the meaning of the term "increasing production," and have provided support for the term in Examples 1 and 2 and Tables 1 through 7. The term "increasing production" is described on page 10, lines 34-37:

The term "increasing production of alcohol" refers to any increase in the yield of alcohol, *e.g.*, ethanol, the volumetric productivity of a fermentation reaction, or the rate of production of alcohol, *e.g.*, ethanol, from a fermentation reaction over a certain period of time or at the completion of the fermentation reaction, as compared to a control.

As is well known in the art, comparison to a control is the standard by which differences in results obtained from the experimental conditions are measured. This is taken to mean that any difference in the amount of ethanol produced is "increased production" as compared to a control cell.

Applicants further define the term "volumetric productivity" on page 10, lines 38-39 through to page 11, lines 1-2, to explain how the increases in production are measured:

The term "volumetric productivity" includes the increased productivity of a cell culture where the productivity of the cells is typically measured as an increase in the amount of a cell derived product in a given cell culture volume, preferably, *e.g.*, an increase in the amount of alcohol produced in grams per liter of culture (*i.e.*, g/L).

In re application of: Lonnie O. Ingram et al.  
Application No.: 09/885,294  
Group No.: 1651  
Filed: June 19, 2001  
Response to Office Action

Applicants note that the claims are read in light of the specification which in turn is directed to one of ordinary skill in the art. Applicants submit that the terms, as described in the forgoing excerpts from the specification and exemplified by the data presented in Examples 1 and 2 and Tables 1 through 7, are sufficiently particular and distinct so that one of ordinary skill in the art would readily understand what is meant by the term "increased production". Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claims 3, 6-9, 18-33, and 38-42 are rejected as incomplete because they depend on a non-elected claim. Applicants have amended the claims to remove the dependence on a non-elected claim. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claim 9 is rejected as being incomplete in the omission of the ATCC number. As noted above, Applicants have amended claim 9 to include the ATCC number. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claim 1 is rejected as being confusing in the recitation of "exposing" as a process step. The Examiner alleges that it is unclear whether there is "contact" with the compound. The extent of "exposure" is not clearly delineated." Applicants respectfully disagree and traverse.

Applicants describe the term "exposing" in the specification on page 11, lines 7-8:[t]he term "exposing" includes contacting the cell with a nutrient compound, *e.g.*, acetylaldehyde from any source. The cell may or may not be in aqueous solution." An example of the conditions for "exposing" a cell with a nutrient compound are described on page 20, lines 12 –32 and on page 21 lines 1-6. Media, nutrients, times of addition of compounds to the culture, *i.e.* "exposing" the cell to the nutrient compound, *etc.* are all fully described. Applicants also describe in great detail the exposure conditions, such as in Example 1, page 21 beginning on line 15. See for example, page 21, lines 15-31.

In re application of: Lonnie O. Ingram et al.

Application No.: 09/885,294

Group No.: 1651

Filed: June 19, 2001

Response to Office Action

Applicants submit that in view of the above excerpt from the specification and Example 1, term "exposing" is sufficiently defined and delineated. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

***Claims Rejections – 35 U.S.C. §102***

Claims 1, 3-4, 6-13, 18-33, and 36-42 are rejected under 35 U.S.C. §102(e) as being anticipated by Ingram '076. Applicants disagree and respectfully traverse. However, without acquiescing to the rejection and in order to expedite prosecution of the application, claim 1 has been amended by deleting OH from the definition of R<sub>1</sub> in formula I. Corresponding amendments have been made to claim 10, and claims 12, 13 and 20 have been cancelled without prejudice or disclaimer. Accordingly, Applicants submit that the rejection no longer applies to claims 1 and 10, and the claims depending therefrom, and respectfully request reconsideration and withdrawal of the rejection.

Claims 1, 3-4, 6-9, 22-27, 29-33. and 36-42 are rejected under 35 U.S.C. §102(b) as being anticipated by Takahashi *et al.* Applicants disagree and respectfully traverse. However, without acquiescing to the rejection and in order to expedite prosecution of the application, claim 1 has been amended by deleting OH from the definition of R<sub>1</sub> in formula I. Corresponding amendments have been made to claim 10, and claims 12, 13 and 20 have been cancelled without prejudice or disclaimer. Accordingly, Applicants submit that the rejection no longer applies to claims 1 and 10, and the claims depending therefrom, and respectfully request reconsideration and withdrawal of the rejection.

Claims 1, 3-4, 13, 22-24, 27, 29-33, 36-40 and 42 are rejected under 35 U.S.C. §102(b) as being anticipated by Albers *et al.* Applicants disagree and respectfully traverse the rejection. However, without acquiescing to the rejection and in order to expedite prosecution of the application, claim 1 has been amended by deleting OH from the definition of R<sub>1</sub> in formula I.

In re application of: Lonnie O. Ingram et al.  
Application No.: 09/885,294  
Group No.: 1651  
Filed: June 19, 2001  
Response to Office Action

Corresponding amendments have been made to claim 10, and claims 12, 13 and 20 have been cancelled without prejudice or disclaimer. Accordingly, Applicants submit that the rejection no longer applies to claims 1 and 10, and the claims depending therefrom, and respectfully request reconsideration and withdrawal of the rejection.

Claims 1, 3, 4, 22-25, 27, 29-33, 40 and 42 are rejected under 35 U.S.C. §102(b) as being anticipated by Quratulain *et al.* Applicants disagree and respectfully traverse. However, without acquiescing to the rejection and in order to expedite prosecution of the application, claim 1 has been amended by deleting OH from the definition of R<sub>1</sub> in formula I. Corresponding amendments have been made to claim 10, and claims 12, 13 and 20 have been cancelled without prejudice or disclaimer. Accordingly, Applicants submit that the rejection no longer applies to claims 1 and 10, and the claims depending therefrom, and respectfully request reconsideration and withdrawal of the rejection.

#### ***Claims Rejections – 35 U.S.C. §103***

Claims 1, 3-4, 6-13, 18-33, and 36-42 are rejected under 35 U.S.C. §103(a) as being unpatentable over Takahashi *et al.* taken with Ingram. Applicants disagree and respectfully traverse. However, without acquiescing to the rejection and in order to expedite prosecution of the application, claim 1 has been amended by deleting OH from the definition of R<sub>1</sub> in formula I. Corresponding amendments have been made to claim 10, and claims 12, 13 and 20 have been cancelled without prejudice or disclaimer. Accordingly, Applicants submit that the rejection no longer applies to claims 1 and 10, and the claims depending therefrom, and respectfully request reconsideration and withdrawal of the rejection.

Claims 1, 3-4, 6-10, 13, 22-27, 30-36, 38-42 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 6,130,076. Applicants disagree and respectfully traverse. However, without acquiescing to the rejection and in order to expedite prosecution of the application, claim 1 has

In re application of: Lonnie O. Ingram et al.  
Application No.: 09/885,294  
Group No.: 1651  
Filed: June 19, 2001  
Response to Office Action

been amended by deleting OH from the definition of R<sub>1</sub> in formula I. Corresponding amendments have been made to claim 10, and claims 12, 13 and 20 have been cancelled without prejudice or disclaimer. Accordingly, Applicants submit that the rejection no longer applies to claims 1 and 10, and the claims depending therefrom, and respectfully request reconsideration and withdrawal of the rejection.

### CONCLUSION

In view of the foregoing, reconsideration and withdrawal of all rejections and allowance of the application with claims 1, 3-4, 6-11, 18, 19, 21-33, and 36-42 are respectfully solicited. If there are any remaining issues or the Examiner believes that a telephone conversation with the Applicants' attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at telephone number shown below.

Respectfully submitted,

EDWARDS & ANGELL, LLP

By   
Peter C. Lauro

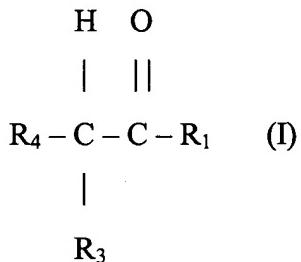
Peter C. Lauro, Esq.  
Reg. No. 32,360  
101 Federal Street  
Boston, MA 02110  
(617) 517-5509

Date: November 26, 2003

In re application of: Lonnie O. Ingram et al.  
Application No.: 09/885,294  
Group No.: 1651  
Filed: June 19, 2001  
Response to Office Action

## APPENDIX A

Claim 1. A method for increasing production of alcohol from a saccharide source by an alcohologenic cell comprising,  
contacting a saccharide source with an alcohologenic cell, and  
exposing said cell to at least one compound of formula I,



wherein;

$\text{R}_1$  is H, or  $\text{COOR}_2$ ;

$\text{R}_2$  is H or alkyl;

$\text{R}_3$  is H,  $\text{NH}_2$ , alkyl or alkenyl;

$\text{R}_4$  is H, alkyl, alkenyl, or a side chain of a naturally occurring amino acid; and salts thereof;

wherein said exposing results in the increased production of alcohol by the alcohologenic cell as compared to a control.

Claim 3. The method of claim 1, wherein said compound of formula I is selected from the group consisting of lower aliphatic aldehydes, lower aliphatic  $\alpha$ -keto carboxylic acids, and salts of any of said acids.

Claim 4. The method of claim 1, wherein said alcohol is ethanol and said alcohologenic cell is an ethanologenic cell.

Claim 6. The method of claim 4, wherein said cell is selected from the family Enterobacteriaceae.

Claim 7. The method of claim 6, wherein said cell is *Escherichia* or *Klebsiella*.

Claim 8. The method of claim 7, wherein said cell is a recombinant cell.

Claim 9. The method of claim 8, wherein said cell is selected from the group consisting of *E. coli* KO4 (ATCC 55123), *E. coli* KO11 (ATCC 55124), *E. coli* KO12 (ATCC 55125), *K. oxytoca* M5A1 (ATCC 68564), *K. oxytoca* P2 (ATCC 55307), and *E. coli* LY01 (ATCC 11303).

Claim 10. The method of claim 4, wherein said compound of formula I is selected from the group consisting of acetaldehyde, and  $\alpha$ -ketoglutarate.

Claim 11. The method of claim 10, wherein said compound of formula I is acetaldehyde.

Claim 18. The method of claim 10, wherein said cell is exposed to glutamate and acetaldehyde.

Claim 19. The method of claim 10, wherein said cell is exposed to pyruvate and acetaldehyde.

Claim 21. The method of claim 10, wherein said cell is exposed to  $\alpha$ -ketoglutarate and succinate.

Claim 22. The method of claim 1, further comprising providing said cell in an aqueous solution.

In re application of: Lonnie O. Ingram et al.  
Application No.: 09/885,294  
Group No.: 1651  
Filed: June 19, 2001  
Response to Office Action

Claim 23. The method of claim 1, wherein said saccharide source is selected from the group consisting of celooligosaccharide, lignocellulose, hemicellulose, cellulose, pectin, xylose, glucose, and any combination thereof.

Claim 24. The method of claim 1, wherein said cell is exposed to said compound of formula I for a period of time between about 1 and about 96 hours.

Claim 25. The method of claim 1, wherein said method is performed at a pH between about 6 and about 8.

Claim 26. The method of claim 25, wherein said method is performed at a pH of about 6.5.

Claim 27. The method of claim 1, wherein said method is performed at a temperature between about 20° and about 40° C.

Claim 28. The method of claim 27, wherein said method is performed at a temperature of about 35° C.

Claim 29. The method of claim 1, wherein said compound is present at a concentration between about 0.1 and about 4.0 g/L.

Claim 30. The method of claim 1, further comprising exposing said cell to said compound more than once.

Claim 31. The method of claim 1, further comprising exposing said cell to two or more different compounds of formula I.

Claim 32. The method of claim 31, wherein said exposing of said cell to said compound is performed at time intervals between about 1 hour and about 24 hours.

In re application of: Lonnie O. Ingram et al.  
Application No.: 09/885,294  
Group No.: 1651  
Filed: June 19, 2001  
Response to Office Action

Claim 33. The method of claim 1, further comprising agitating said cell, said saccharide source, and said compound between about 50 rpm and about 200 rpm.

Claim 38. The method of claim 1, wherein said method is performed in a fermentor vessel.

Claim 39. The method of claim 38, wherein said cell and said saccharide source are provided in an aqueous solution.

Claim 40. The method of claim 39, wherein said aqueous solution comprises a fermentation medium.

Claim 41. The method of claim 40, wherein said fermentation medium comprises Luria broth or CSL broth.

Claim 42. The method of claim 1, wherein said method is suitable for simultaneous saccharification and fermentation.

BOS2\_355958.1